U.S. FOOD & DRUG ADMINISTRATION

Human Foods Program

Yue Yang, Ph.D.
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Shanghai 201203
CHINA

Re: GRAS Notice No. GRN 001275

Dear Dr. Yang:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001275. We received Cataya Bio (Shanghai) Co., Ltd. (Cataya)'s notice on May 1, 2025, and filed it on August 11, 2025. Cataya submitted amendments to the notice on January 12, 2026, February 2, 2026, and March 19, 2026, that clarified the intended use, manufacturing, specifications, dietary exposure, and aspects of the safety narrative.

The subject of the notice is 6′-sialyllactose sodium salt (6′-SL) for use as an ingredient in foods, including infant formula, at the maximum levels shown in Table 1. Cataya states that 6′-SL is not intended for use in products under the U.S. Department of Agriculture's jurisdiction or in foods for which standards of identity do not permit its addition. The notice informs us of Cataya's view that these uses of 6′-SL are GRAS through scientific procedures.

Table 1: Intended food categories and use levels for 6′-SL

Food Categories	Maximum Use Levels (g/kg or g/L)
Non-exempt infant formula for term infants[1]	0.4
Formula intended for young children (>12 months)	0.5
Breads and baked goods, including gluten-free	10
Soft drinks (regular and diet)	0.25
Enhanced, fortified waters, and flavored waters (including carbonated waters)	0.25
Meal replacement drinks, non-milk based	1
Sports, isotonic, and "energy" drinks	0.5
Protein drinks	1
Hot breakfast cereals, instant and ready-to-eat (RTE)	1

[1] Cataya states that the use of 6′-SL in non-exempt infant formula is not restricted to any specific protein base (e.g., cow milk-based, soy-based).

RTE breakfast cereals, puffed	17
RTE breakfast cereals, high-fiber	6.2
RTE breakfast cereals, biscuit-type	4.2
Chewing gum	62
Coffee and tea	2.1
Milk substitutes	0.25
Beverage whiteners	125
Non-dairy cream	125
Non-dairy yogurts	2.2
Frozen dairy-based desserts (including ice creams and frozen yogurts, frozen novelties)	3.5
Edible ices, sherbet and sorbet	3.5
Milk-based puddings, custards, and mousses (including gelatin desserts)	3.5
Fruit pie filling	2.9
Fruit filling in bars, cookies, yogurt, and cakes	6.25
Cereal and granola bars, including “energy,” protein, and meal replacement bars	10
Hot cereals for infants and young children, prepared (from dry instant) and ready-to-serve	2.3
Other foods for infants and young children	2.5
Other drinks for young children	0.25-2.1
Desserts including fruit desserts, cobblers, and yogurt/fruit combinations (“junior type desserts”)	2.3
Crackers, pretzels, cookies, and other snack items for infants and young children	12
Jams, jellies, fruit preserves, and fruit butters	12
Unflavored pasteurized and sterilized milk; whole milk, reduced-fat milk, low-fat milk, non-fat milk (including powdered milks, reconstituted)	0.5
Buttermilk	0.25
Flavored milk	0.25
Evaporated and condensed milk	0.25
Meal replacement for weight management, milk-based	1
Yogurt	5
Fruit juices and nectars	0.25
Fruit-flavored drinks and ades	0.25
Canned fruits	3.5
Fruit-based desserts	3.5
Vegetable juices and nectars	0.25
Sugar substitutes: table-top sweeteners	62
Syrups used to flavor milk beverages	1.5
Nutritional drinks for pregnant women, milk-based	12.5
Oral nutritional drinks, milk-based	1.68
Formula for enteral tube feeding (11 years and older)	4.1

Cataya provides information on the identity and composition of 6′-SL (CAS Registry Number 157574-76-0). Cataya describes 6′-SL as a white to ivory powder consisting of ≥90% 6′- SL on a dry weight (DW) basis and small quantities of other related carbohydrates (6′-sialyllactulose, D-lactose, and *N*-acetyl-D-neuraminic acid sialic acid). 6′-SL is a trisaccharide consisting of sialic acid and lactose linked through an α-2,6 glycosidic linkage. Cataya states that 6′-SL is chemically and structurally equivalent to the 6′-SL in human milk, as confirmed by nuclear magnetic resonance spectroscopy.

Cataya describes the production organism used in the manufacturing process for 6′-SL. The production organism, *Corynebacterium glutamicum* CGMCC 7.577, is constructed through genetic engineering of the *C. glutamicum* DSM 20300 parent strain by insertion of six heterologous genes to allow production of 6′-SL from D-glucose or D-sucrose and D-lactose. Cataya states that all genetic modifications are verified by polymerase chain reaction, Sanger sequencing, and whole genome sequencing, and that the strain is non-pathogenic and non-toxigenic. The production strain is deposited in the China General Microbiological Culture Collection under the deposit number CGMCC 7.577.

Cataya describes the two-stage manufacturing process, which includes an upstream fermentation stage and a downstream purification stage. In the first stage, 6′-SL is produced from D-glucose (or D-sucrose) and D-lactose by fermentation with *C. glutamicum* CGMCC 7.577 in a stirring-type reactor under controlled conditions and is secreted into the fermentation medium. After fermentation is complete, the production organism is inactivated and removed by microfiltration. The filtrate containing 6′-SL undergoes a series of purification steps. First, the filtrate undergoes a series of cationic and anionic resin exchanges to eliminate cations, anions, minerals, and organic impurities. The resulting solution is concentrated by nanofiltration, purified using activated charcoal to remove color and organic matter, and then concentrated through evaporation. The concentrated solution is filtered using an ultrafiltration membrane to remove endotoxins, residual proteins, organic impurities, and microbial contaminants. The purified solution is spray dried to obtain the final 6′-SL. Cataya states that 6′-SL is manufactured according to current good manufacturing practices, and that all raw materials and processing aids are food-grade and are used in accordance with applicable U.S. regulations, are GRAS for their intended uses, or are the subject of an effective food contact notification.

Cataya provides specifications for 6′-SL, which include the minimum content of 6′-SL sodium salt (≥90% DW) and limits on D-lactose (≤3% DW), *N*-acetyl-D-neuraminic acid (≤2%), 6′-sialyllactulose (≤5% DW), moisture (≤10.5%), protein (≤0.01% w/w), sodium (2.5%-4.2%), heavy metals (including lead (≤0.02 mg/kg)), cereulide (<0.5 µg/kg), and microorganisms, including *Salmonella serovars* (absent in 25 g), *Listeria monocytogenes* (absent in 25 g), and *Cronobacter sakazakii*. Cataya provides the results from five non-consecutive batch analyses to demonstrate that 6′-SL can be manufactured to meet the specifications. Cataya provides the results from an accelerated stability study demonstrating that 6′-SL is stable at 40 °C and 75% relative humidity for at least 13 weeks and indicates that because of the compositional similarity,

the stability of 6′-SL is expected to be similar to 6′-SL described in GRNs 000881 and 001053.[2]

Cataya states that the intended uses of 6′-SL are substitutional for those described in GRN 001053 and incorporates into the notice those dietary exposure estimates. Cataya states that the estimated eaters-only dietary exposure to 6′-SL is 0.49 g/person (p)/d (74 mg/kg body weight (bw)/d) at the mean and 0.90 g/p/d (119 mg/kg bw/d) at the 90th percentile for infants aged 0-6 months, and 1.0 g/p/d (110 mg/kg bw/d) at the mean and 1.74 g/p/d (190 mg/kg bw/d) at the 90th percentile for infants aged 7-12 months. For children aged 1-3 years, the estimated eaters-only dietary exposure to 6′-SL is 1.06 g/p/d (77 mg/kg bw/d) and 1.69 g/p/d (134 mg/kg bw/d) at the mean and 90th percentile, respectively. For the U.S. population aged 2 years and older, the estimated eaters-only dietary exposure to 6′-SL is 1.95 g/p/d (30 mg/kg bw/d) and 3.6 g/p/d (64 mg/kg bw/d) at the mean and 90th percentile, respectively. Cataya notes that because the intended uses of 6′-SL are substitutional for the current uses of other sources of 6′-SL, an increase in the cumulative dietary exposure to 6′-SL is not expected.

Cataya discusses dietary exposure to 6′-SL from the intended use in oral nutritional drinks that are intended for the general population (aged 2 years and older). Cataya estimates the dietary exposure to 6′-SL to be 0.84 g/p/d based on the intended use level of 1.68 g/L and an estimated consumption rate of two 250 mL servings/d. Cataya also discusses dietary exposure to 6′-SL from the intended use in formula for enteral tube feeding for children aged 11 years and older and estimates dietary exposure to be 2.0 g/p/d based on the intended use level of 4.1 g/L and an estimated consumption rate of two 250 mL servings/d.

Cataya discusses data and information to support safety, including that the subject of this notice is chemically and structurally equivalent to 6′-SL in human milk, and is compositionally similar to preparations of 6′-SL that were the subjects of GRNs 000881, 000922, 001053, and 001075.[2] Cataya states that the intended uses and dietary exposure estimates are identical to those in GRN 001053, and are supported by published safety studies, including *in vitro* and *in vivo* genotoxicity studies, subchronic oral toxicity studies in rats, and preclinical studies in neonatal piglets. Cataya states that in previous GRNs that received no questions letters, the safety and tolerance of using 6′-SL in infant formula for term infants was concluded to be GRAS at concentrations of up to 0.4 g/L. Cataya discusses new studies identified in a literature search through December 2025, and concludes that no new publicly available data and information would contradict its GRAS conclusion.

Based on the totality of the data and information, Cataya concludes that 6′-SL is GRAS for its intended use.

[2] 6′-SL was the subject of GRNs 000881, 000922, 001053, and 001075. We evaluated these notices and responded in letters dated February 24, 2020, April 23, 2021, May 12, 2023, and March 22, 2023, respectively, stating that we had no questions at that time regarding the notifiers' GRAS conclusions.

Standards of Identity

In the notice, Cataya states its intention to use 6′-SL in several food categories, including foods for which standards of identity exist, located in Title 21 of the CFR. We note that an ingredient that is lawfully added to food products may be used in a standardized food only if it is permitted by the applicable standard of identity.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, & Cosmetic (FD&C) Act, a food is misbranded if its labeling is false or misleading in any way. Section 403(r) of the FD&C Act lays out the statutory framework for labeling claims characterizing a nutrient level in a food or the relationship of a nutrient to a disease or health-related condition (also referred to as nutrient content claims and health claims). If products containing 6′-SL bear any nutrient content or health claims on the label or in labeling, such claims are subject to the applicable requirements and are under the purview of the Office of Nutrition and Food Labeling (ONFL) in the Nutrition Center of Excellence (NCE). The Office of Pre-Market Additive Safety (OPMAS) did not consult with ONFL on this issue or evaluate any information in terms of labeling claims. Questions related to food labeling should be directed to ONFL.

Allergen Labeling

The FD&C Act requires that the label of a food that is or contains an ingredient that contains a "major food allergen" declare the allergen's presence (section 403(w)). The FD&C Act defines a "major food allergen" as one of nine foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, soybeans, and sesame) or a food ingredient that contains protein derived from one of those foods. 6′-SL derived from lactose may require labeling under the FD&C Act because it may contain protein derived from milk. Questions about petitions or notifications for exemptions from the food allergen labeling requirements should be directed to the Division of Food Ingredients in OPMAS. Questions related to food labeling in general should be directed to ONFL.

Intended Use in Infant Formulas

Under section 412 of the FD&C Act, a manufacturer of a new infant formula must make a submission to FDA providing required assurances about the formula at least 90 days before the formula is marketed. Our response to Cataya's GRAS notice does not alleviate the responsibility of any infant formula manufacturer that intends to market an infant formula containing 6′-SL to make the submission required by section 412. Infant formulas are the purview of the Office of Critical Foods in NCE.

Section 301(ll) of the FD&C Act

Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction

into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ll)(1)-(4) applies. In our evaluation of Cataya's notice concluding that 6′-SL is GRAS under its intended conditions of use, we did not consider whether section 301(ll) or any of its exemptions apply to foods containing 6′-SL. Accordingly, our response should not be construed to be a statement that foods containing 6′-SL, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Cataya provided, as well as other information available to FDA, we have no questions at this time regarding Cataya's conclusion that 6′-SL is GRAS under its intended conditions of use. This letter is not an affirmation that 6′-SL is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient manufacturers and food producers are responsible for ensuring that marketed products are safe and compliant with all applicable legal and regulatory requirements.

In accordance with 21 CFR 170.275(b)(2), the text of this letter responding to GRN 001275 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

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